REMARKS

Claim 48 has been amended and further specifies the disintegrating agents as mentioned in former claim 54 (which has been deleted).

Claims 48-74 are rejected under 35USC§112, first paragraph, as containing subject matter which are not described in the specification.

Claims 48 and 61 have been amended to overcome said objection by deleting the expression "said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid".

Said expression had been introduced in response to the previous office action, however, it was not necessary to confer novelty of the claim. Consequently, it can be cancelled without prejudice.

Claims 60 and 74 are objected to because there is insufficient antecedent basis for the limitation "sweetener".

The dependency of these claims has been amended in order to overcome said objection.

Claims 48-50, 53, 55-56, 59-63, 65, 67-70, 73 and 74 are rejected under 35 USC 102(e) as being anticipated by Gowan (US5,876,759).

Applicants respectfully disagree.

The Examiner indicates that "Gowan discloses a rapidly disintegrating tablet (30 seconds or less) containing coated acetaminophen (23%), mannitol (57%), microcrystalline cellulose (15%), aspartame, colloidal silicon dioxide (.06%) and stearic acid (.75%)."

Said disclosure corresponds in fact to the example of Gowan.

In claim 48 as amended, it is specified that the disintegration agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof. Those specific disintegrating agents are not mentioned in Gowan.

Claim 48 is thus novel in view of Gowan.
Since claims 49 to 53 and 55 to 60 depend on claim 48, they are also novel.

In claim 61, it is specified that at least two carbohydrates are used which present different particle sizes. Such a feature is not disclosed in Gowan.

Claim 61 and depending claims 62-74 are thus novel in view of Gowan.

Claims 48-53, 55-57, 69-71, 73 and 74 are rejected under 35 USC §103(a) as being obvious over Gowan (US5,876,759).

The Examiner considers that by routine optimization with the expectation of similar results, the man of ordinary skill can obtain the tablet according to the invention using Gowan teaching.

Applicants respectfully disagree.

In fact, as indicated in Mr Noureddine's Declaration under rule 132, which is herewith attached (as a facsimile copy), Gowan's oral formulations do not contain a disintegration agent. In fact, microcrystalline cellulose, when used in a low concentration (less than about 30 %) cannot act as a disintegrating agent but as a binder.

Furthermore, the use of microcrystalline cellulose is specifically mentioned as being a use as a binder agent which is used "to add cohesiveness to the formulation" (see Gowan column 3, lines 26-27).

There is no incentive in Gowan to add a disintegrating agent to the formulation agent to the formulation containing a binder.

Furthermore, the specific disintegrants of claim 48 are nor described nor suggested.

Claim 48 and depending claims 49-53, 55-60 are thus inventive in view of Gowan.

The use of two specific polyols presenting specified granulometry used as binders is not disclosed nor suggested in Gowan.

Claim 61, and depending claims 62-74 are thus inventive in view of Gowan.

Claims 54, 56-57, 68, 71-72 are rejected under 35 USC 103(a) as being unpatentable over Gowan (US5,876,759)in view of Ku et al. (US5,994,348).

Applicants respectfully disagree.

The Examiner considers that "*it would have been obvious to one of ordinary skill in the art at the time the invention was made to look to the teachings of Ku et al. since Ku teaches rapidly disintegrating tablets with similar excipients for rapid dissolution.*"
However, it clearly appears in Ku et al. that the tablets are intended to be swallowed, i.e., the disintegrating properties are not disintegrating properties into the buccal cavity as in the present invention, but once swallowed.

Furthermore, in the tablets according to Ku et al., the active substance is not under coated form.

Consequently, Ku et al. teaches away from the invention.

In view of said intended use, the person with ordinary skill in the art would not be incited to combine Gowan with Ku et al.

In particular, the person with skill in the art will not be incited to introduce silicon dioxide into the composition of Gowan because said product is indicated in Ku et al. as being a "antiadherent" capable of reducing the stickiness of the formulation, said stickiness of the formulation resulting from the specific active substance used in Ku et al. which is "sticky and can adhere to surfaces" as indicated at column 1 lines 53-54.

In Gowan, there is no such problem of stickiness since the particles of active substance are coated.

Thus the man skilled in the art is not incited to add silicon dioxide or similar compounds to Gowan's composition. And even if he add them he will never obtain the tablet according to the invention.

Claims 48 and 61 are thus inventive over Gowan in view of Ku et al.
Since claims 49-53 and 55-60, 62-74 depend respectively on claims 48 and 61, they are also inventive.

Claims 48-52, 54-59, 61-66, 68-73 are rejected under 35 USC 103(a) as being unpatentable over Liu et al. (US6,465,009).

The Examiner considers in fact that it would be obvious to one of ordinary skill in the art to combine Liu et al. and Ku et al. in order to obtain the tablet according to the invention.

Applicants respectfully disagree.

In fact, Liu et al. teaches the use of a non-saccharide water-soluble binder in order to increase the disintegration of a tablet. Such a non-saccharide water soluble binder is polyvinylpyrrolidone.

Liu et al. does not teach the use of a permeabilizing agent and does not indicate the amount of disintegration agent which can optionally be used.

Ku et al., as already indicated, described tablets which are intended to be swallowed and not to disintegrate in the buccal cavity in contact with saliva, and in which the active substance is not coated.

As indicated by the Examiner, Ku et al. uses anti-adherent such as silicon dioxide in order to reduce the stickiness of the formulation. However, it is important to underline that said stickiness is due to the specific active substances which are used.

While, in Liu et al. there is no such a problem of stickiness of the active substance, and even if it exists the coating of the active substance solves said problem.

Consequently, the person skilled in the art is not incited to combine those two documents. And even if the man skilled in the art would combine said documents, he will never obtain the tablet according to the invention.

Claims 48 and 61 are thus inventive over Gowan in view of Ku et al.
Since claims 49-53 and 55-60, 62-74 depend respectively on claims 48 and 61, they are also inventive.

It is submitted that the application is now in proper form for allowance and favourable consideration is respectfully submitted.

Respectfully submitted

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Marked-up version of the claims

48. (amended) Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent selected from the group consisting of croscarmellose, crospovidone and mixtures thereof; a soluble diluent agent with binding properties which consists of a directly compresssible polyol having less than 13 carbon atoms, with an average particle diameter of 100 to 500 µm; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet[,].

[said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid.]

49. Improved multiparticulate tablet according to claim 48, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

50. Improved multiparticulate tablet according to claim 48, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol and maltitol.

51. Improved multiparticulate tablet according to claim 48, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

52. Tablet according to claim 48, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

53. Tablet according to claim 48, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

54. (deleted) [Tablet according to claim 48, wherein the disintegrating agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof.]

55. Tablet according to claim 48, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

56. Tablet according to claim 55, wherein the permeabilizing agent is precipitated silica.

57. Tablet according to claim 48, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

58. Tablet according to claim 48, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

59. Tablet according to claim 48, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

60. (amended) Tablet according to claim [50] 49, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.

~~61.~~ (amended) Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; at least two soluble diluent agents with binding properties which consists of a polyol having less than 13 carbon atoms and at least one diluent agent being in the form of the directly compressible product with an average particle diameter of 100 to 500 µm, and at least one diluent agent being in the form of a powder with an average particle diameter of less than 100µm, the ratio of directly compressible polyol to powder polyol being 99/1 to 20/80; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet[,]. [said active principle not being intimately dispersed or dissolved in a pharmaceutically acceptable lipid.]

62. Improved multiparticulate tablet according to claim 61, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

63. Improved multiparticulate tablet according to claim 61, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol, sorbitol and maltitol.

64. Improved multiparticulate tablet according to claim 61, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

65. Improved multiparticulate tablet according to claim 61, wherein the proportion of directly compressible polyol to powder polyol is 80/20 to 20/80.

66. Tablet according to claim 61, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

67. Tablet according to claim 61, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

68. Tablet according to claim 61, wherein the disintegrating agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof.

69. Tablet according to claim 61, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

70. Tablet according to claim 69, wherein the permeabilizing agent is precipitated silica.

71. Tablet according to claim 61, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

72. Tablet according to claim 71, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

73. Tablet according to claim 61, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

74. (amended) Tablet according to claim [63] 62, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.

Clean version of the claims

48. (amended) Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent selected from the group consisting of croscarmellose, crospovidone and mixtures thereof; a soluble diluent agent with binding properties which consists of a directly compresssible polyol having less than 13 carbon atoms, with an average particle diameter of 100 to 500 µm; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet.

E1

49. Improved multiparticulate tablet according to claim 48, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

50. Improved multiparticulate tablet according to claim 48, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol and maltitol.

51. Improved multiparticulate tablet according to claim 48, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

52. Tablet according to claim 48, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

53. Tablet according to claim 48, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

54. (deleted)

55. Tablet according to claim 48, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

56. Tablet according to claim 55, wherein the permeabilizing agent is precipitated silica.

57. Tablet according to claim 48, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

58. Tablet according to claim 48, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

59. Tablet according to claim 48, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

60. (amended)Tablet according to claim 49, wherein the sweetener is selected from the group consisting of aspartame,

potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.

61. (amended) Improved multiparticulate tablet which disintegrates in contact with the saliva in the mouth in less than 40 seconds, wherein it is based on particles of coated active principle which have intrinsic compression characteristics, and on a mixture of excipients being free of effervescent agents and the ratio of excipient mixture to coated active principle particles being 0.4 to 6 parts by weight, the mixture of excipients comprising: a disintegration agent; at least two soluble diluent agents with binding properties which consists of a polyol having less than 13 carbon atoms and at least one diluent agent being in the form of the directly compressible product with an average particle diameter of 100 to 500 µm, and at least one diluent agent being in the form of a powder with an average particle diameter of less than 100µm, the ratio of directly compressible polyol to powder polyol being 99/1 to 20/80; a lubricant; a permeabilizing agent, the proportion of disintegration agent being 1 to 15% by weight and the proportion of soluble agent being 30 to 90% by weight, based in each case on the weight of the tablet.

62. Improved multiparticulate tablet according to claim 61, wherein the mixture of excipients further comprises lubricants, sweeteners, flavorings and colors.

63. Improved multiparticulate tablet according to claim 61, wherein the polyol having less than 13 carbon atoms is selected from the group consisting of mannitol, xylitol, sorbitol and maltitol.

64. Improved multiparticulate tablet according to claim 61, wherein the ratio of excipient mixture to coated active principle is 1 to 4 parts by weight.

65. Improved multiparticulate tablet according to claim 61, wherein the proportion of directly compressible polyol to powder polyol is 80/20 to 20/80.

66. Tablet according to claim 61, wherein the proportion of disintegration agent is 2 to 7% by weight and the proportion of soluble agent is 40 to 70% based in each case on the weight of the tablet.

67. Tablet according to claim 61, wherein the active principle is selected from the group consisting of aspirin, paracetamol and ibuprofen.

68. Tablet according to claim 61, wherein the disintegrating agent is selected from the group consisting of croscarmellose, crospovidone and mixtures thereof.

69. Tablet according to claim 61, wherein the permeabilizing agent is selected from the group consisting of silicas with a high affinity for aqueous solvents, maltodextrins, β-cyclodextrines and mixtures thereof.

70. Tablet according to claim 69, wherein the permeabilizing agent is precipitated silica.

71. Tablet according to claim 61, wherein the proportion of permeabilizing agent is 0.1 to 10% based on the weight of the tablet.

72. Tablet according to claim 71, wherein the proportion of permeabilizing agent is 0.5 to 5% based on the weight of the tablet.

73. Tablet according to claim 61, wherein the lubricant is selected from the group consisting of magnesium stearate, sodium stearyl flumarate, stearic acid, micronized polyoxyethylene glycol and mixtures thereof.

E3

74. (amended) Tablet according to claim 62, wherein the sweetener is selected from the group consisting of aspartame, potassium acesulfame, sodium saccharinate, neohesperidin dihydrochalcone and mixtures thereof.